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PHASE 3 SUMMARY OF MRID 00093999:

ACUTE DERMAL TOXICITY IN THE RABBIT

STUDY # 6818A

FLUMETRALIN

GUIDELINE REFERENCE:

81-2 ACUTE DERMAL TOXICITY IN THE RABBIT

SUMMARY PREPARED BY:

JACQUELINE GILLIS, Ph.D.

MERRILL TISDEL

14 SEPTEMBER 1990

ORIGINAL STUDY PREPARED BY:

FOOD AND DRUG RESEARCH LABORATORIES, INC.

WAVERLY, NEW YORK

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1)(A), (B), or (C).

Company: CIBA-GEIGY Corporation (Typed Name)

Company Agent: Thomas Parshley (Typed Name)

Title: Senior Reg. Specialist

Signature: _____ Date: _____

These data are the property of the Agricultural Division of CIBA-GEIGY Corporation, and as such, are considered to be confidential for all purposes other than compliance with FIFRA §10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality which may exist under any other statute or in any other country.

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FDRL Study No. 6818A

Acute Dermal Toxicity Study in Rabbits
of CGA-41065 Technical

GLP Compliance Statement

I hereby certify that this study was performed in compliance with regulations for Good Laboratory Practice (GLP) as described by FDA (21 CFR Part 58) and although completed and reported prior to promulgation of the EPA GLP, essentially in compliance with EPA (40 CFR Part 160).

James Laveglia, ~~Ph.D.~~, President
for Study Director

9/6/90
Date

This study does not meet the requirements for 40 CFR Part 160 since it was conducted prior to the issuance of the EPA Good Laboratory Practice Standards. It was conducted according to the FDA Good Laboratory Practice Standards as indicated above.

Submitter/Sponsor of Study:

Merrill Tisdel
Agricultural Division
CIBA-GEIGY Corporation
Greensboro, North Carolina

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Certification of Availability of Raw Data

I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.

Submitter's Representative:

Signature/Date: Merrill Tisdel 10.15.90

Typed Name: Merrill Tisdel

Title: Toxicologist

Certification of Accuracy of Summary and Adequacy of the Study

I certify, in compliance with FIFRA section 4(e)(1)(A), that this summary accurately represents the data presented in the report(s) of this study cited by MRID, and that this study fully satisfies all pertinent requirements of the OPP Guideline it addresses.

Submitter's Representative:

Signature/Date: Merrill Tisdel 10.15.90

Typed Name: Merrill Tisdel

Title: Toxicologist

R406MT0628MG

81-2 Acute Dermal Toxicity in the Rat, Rabbit or Guinea Pig

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. Y — Technical form of the active ingredient tested. (for reregistration only)
2.* Y — At least 5 animals/sex/group
3.* N — Rats 200-300 gm, rabbits 2.0-3.0 kg or guinea pigs 350-450 gm.
4. Y — Dosing, single dermal.
5. Y — Dosing duration at least 24 hours.
6.* NA — Vehicle control, only if toxicity of vehicle is unknown.
7. Y — Doses tested, sufficient to determine a toxicity category or a limit dose (2000 mg/kg).
8. Y — Application site clipped or shaved at least 24 hours before dosing
9. Y — Application site at least 10% of body surface area.
10. N — Application site covered with a porous nonirritating cover to retain test material and to prevent ingestion.
11. Y — Individual observations at least once a day.
12. Y — Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
13. Y — Individual daily observations.
14.* Y — Individual body weights.
15.* Y — Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

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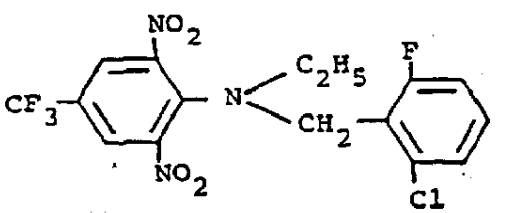
IDENTIFICATION OF TEST MATERIAL

Chemical Name

CAS Name:	N-(2-Chloro-6-fluorobenzyl)-N-ethyl-α,α,α,-trifluoro-2,6-dinitro-p-toluidine
	or
	2-Chloro-N-[2,6-dinitro-4-(trifluoromethyl)phenyl]-N-ethyl-6-fluorobenzenemethanamine
Common Name:	Flumetralin
Trade Name:	Prime +®
CIBA-GEIGY Code Number:	CGA-41065
CAS Registry Number:	62924-70-3
EPA Shaughnessy Number:	Unknown

Chemical Structure:



Percent Active Ingredient

92% minimum

Flumetralin: 81-2: Acute Dermal Toxicity in the Rabbit

1. The test article was Flumetralin (CGA-41065) Technical, a bright orange crystalline substance, FL-810009, purity 96.4%.

2. Five male and five female New Zealand white rabbits were tested at one dose level (a limit dose).

3. Male animals weighed between 2.5-3.0 kg and female animals weighed between 2.1-3.0 kg when tested.

4. The test article was applied to the exposure area on the back and flank of each animal one time.

5. The duration of dermal exposure was 24 hours.

6. No vehicle was used for application of the test article; therefore, a vehicle control was not necessary.

7. Dose tested and results were:

Dose (mg/kg)	Number Dead/Number Treated		
	Males	Females	Overall
2000	1/5	0/5	1/10
LD_{50} (mg/kg)	>2000	>2000	>2000

8. The animals were prepared approximately 24 hours prior to treatment by clipping a portion of the back and flank of each animal free of hair. Immediately prior to application of the test article, the exposure area was abraded with the point of a disposable hypodermic needle. The abrasions penetrated the stratum corneum but did not disturb the derma or cause bleeding.

9. The area of the application site was approximately 30% of the total body surface.

10. Following application of the test material, the application site was covered with an occlusive wrap consisting of a layer of plastic wrap, a protective cloth, and a stockinette sleeve. The wrap was held in place with masking tape.

11. Observations for pharmacologic and/or toxicologic effects and mortality were recorded approximately 2.5 hours after dosing. None of the animals exhibited toxicologic effects on the day of dosing.

12. Individual observations were made twice daily for 14 days after the day of dosing. One male animal died on Day 7, following observations of activity decrease and diarrhea for two days. Signs of nasal discharge, no feces, and soft feces were observed in several animals after Day 7; all surviving animals appeared normal by Day 14.

13. See Items 11 and 12.

14.

Dose (mg/kg)	Body Weights (kg) (Mean/Number Alive)					
	Males			Females		
	Initial	Day 7	Day 14	Initial	Day 7	Day 14
2000	2.69/5	2.68/4	2.75/4	2.70/5	2.85/5	3.05/5

15. A gross necropsy examination was conducted on the animal which died during the study and all surviving animals at study termination. Findings of discolored contents and gas in the intestines were observed in the animal which died and one other animal. No other treatment-related abnormalities were observed.

16. There were no significant changes from the Acceptance Criteria in this study. One deviation from the Acceptance Criteria is noted. Under Item 10, the application site was covered with an occlusive covering rather than a porous covering. This deviation is considered to be insignificant because, in general, the procedure used would tend to enhance absorption and increase whatever toxic effects might develop; even with this possibility of heightened effects, the LD_{50} was >2000 mg/kg.

GILLIS:R502SW0921JG/MT